

Promise Winter 2008

ST. JUDE ON THE DOUBLE

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St. Jude Children's Research Hospital's mission is to advance cures, and means of prevention, for pediatric catastrophic diseases through research and treatment. Consistent with the vision of our founder, Danny Thomas, no child is denied treatment based on race, religion or a family's ability to pay. Hospital Director and Chief Executive Officer William E. Evans, PharmD

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On the cover: Lauren and Kara Lee. Story on page 10; photo by Peter Barta.

Highlights

Better understanding AML

Recent research findings have provided scientists with new insight into the cause of acute myeloid leukemia (AML). This cancer is diagnosed in about 20 percent of children with leukemia. The discovery may also lead to the development of new ways of treating this cancer.

While studying a gene known as *N-Myc*, St. Jude investigators discovered that when this gene is overactive, it can trigger AML if a helper protein called IL-3 is present. When IL-3 is not present, the overactive gene causes the cell to self-destruct.

"This discovery might contribute to new strategies for treating this leukemia or disrupting this gene's ability to cause it," said Gerard Grosveld, PhD, Genetics and Tumor Cell Biology chair. Grosveld is senior author of a report on this work that appeared in the November 2007 issue of *Cancer Research*.

Fighting fatigue

Children undergoing treatment for acute lymphoblastic leukemia (ALL) often suffer fatigue and poor quality of sleep. Recent discoveries by St. Jude researchers indicate that dexamethasone, an anti-leukemic drug used in treating ALL, can cause this common side effect.

Clinicians hope that by developing new methods of administering this drug, they can reduce and even eliminate this problem.

According to Pamela Hinds, RN, PhD, Nursing Research director, health care workers should prepare patients and families to expect an increase in disrupted sleep and fatigue. Hinds is the first author of this study, which appeared in the November 15, 2007, issue of *Cancer*.

Lymphatic breakthrough

St. Jude investigators have discovered the origin of the network of lymphatic vessels critical to various essential housekeeping functions in the body. This finding is a major contribution to work aimed at promoting growth of new vessels in people suffering from different forms of disease that disrupt this system, according to Guillermo Oliver, PhD, of Genetics and Tumor Cell Biology.

The lymphatic system is essential for the immune response to infectious agents, and a defective lymphatic vasculature could also promote obesity. The researchers showed that this network arises in the fetus by means of continuous release from the veins of cells that multiply and then migrate to different parts of the body. Oliver is senior author of a report on this work that appears in the October 1, 2007, issue of *Genes & Development*.

Adaptive styles

Children under treatment for cancer are generally emotionally well-adjusted and no more depressed or anxious than other children their age, according to St. Jude researchers. In studies of depression, anxiety, posttraumatic stress and quality of life, children with cancer do as well as, and often better than, their healthy peers.

"What we are learning from this population might help us learn how to improve the quality of life of children who are not doing so well," said Sean Phipps, PhD, of Behavioral Medicine.

Phipps is the author of an article on adaptive styles in children with cancer that appeared in the December 2007 issue of *Journal of Pediatric Psychology*.

Solving mysteries of ALL

Results of a study by St. Jude investigators shed new light on why a small percentage of children with acute lymphoblastic leukemia (ALL) do not benefit from treatment, while more than 90 percent of children treated with the latest therapies survive.

The findings could help researchers



better understand both the origins of this aggressive form of leukemia (termed Philadelphia chromosome-positive ALL) as well as why it becomes resistant to the targeted anti-leukemia drug imatinib (GleevecTM). This knowledge may lead to more effective treatments for patients who are not helped by current therapies, according to Charles Sherr, MD, PhD, a Howard Hughes Medical Institute investigator and co-chair of Genetics and Tumor Cell Biology. Sherr was senior author and his colleague Richard Williams, Oncology, was first author of a report on these results that appeared in the September 15, 2007, issue of Genes & Development.

Tracking bird flu

St. Jude investigators have found a way to monitor the H5N1 bird flu virus to determine if it is adapting to humans and therefore increasing its ability to trigger a deadly pandemic. The scientists identified specific amino acid building blocks that are more likely to appear in avian influenza virus proteins and those that are more likely to be in human influenza virus proteins. The differences in these amino acids can be used as markers to track changes in H5N1 avian influenza strains that threaten humans.

St. Jude Chief Information Officer Clayton Naeve, PhD, was senior author, and David Finkelstein, PhD, of the Hartwell Center for Bioinformatics and Biotechnology was first author of a report on this work that appeared in the October 2007 issue of *Journal of Virology*.

Your opinion matters

ALSAC would like to hear your comments so that you can continue to have the best St. Jude donor experience possible. E-mail *www.stjude.org/opinion*, call 1-800-822-6344 or write St. Jude/ ALSAC, 501 St. Jude Place, Memphis, TN 38105 to offer your input. ●

Lifelong Commitment

Thanks to one devoted lady, a special area in the Chili's Care Center will house an exciting tool for saving young lives.

By Lynda Nance

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"I'm not a doctor, and I'm not a

scientist. But writing checks is my

way of helping to save lives."

s a child of the Depression, Peachy Schwartz's desire to help others started early. The sight of men on street corners with bushels of apples at their feet made a lasting impression. "Those men were trying to get some money, any way they could," she recalls. "I've just always wanted to give to anyone who needed it."

In the years since then, Schwartz has made helping others a part of her life. "I'm not a doctor, and I'm not a scientist," she says. "But writing checks is my way of helping to save lives."

Before her husband, ST. JUDE Joseph, passed away in 1999, the couple gave to numerous causes. "My husband was a OSPITAL great philanthropist," Schwartz says. "He always said, 'The more you give, the more you get back." In recent years, Schwartz found the place she calls her passion: St. Jude Children's Research Hospital. "I used to watch the programs on TV

and think, 'Children are dying; I've got to do

something," she says. "Danny Thomas' legacy is so beautiful, so magnificent and enriching. It blows me awav."

Initially, Schwartz found out about St. Jude

after receiving a request in the mail. She formed a relationship with her area ALSAC/St. Jude philanthropic adviser, who invited Schwartz to visit the hospital and see the work done there. As a result of that visit, Schwartz's respect and commitment to the organization deepened.

The hospital, Schwartz found, was an upbeat place-one with lots of promise for the future. "St. Jude is my favorite

because it gives these kids a chance to grow into adulthood," she says, "a chance they wouldn't otherwise have." During a tour of the hospital, she was thrilled to see how her donations directly impacted the patients and their care.

Schwartz recently committed to sponsoring a room that houses a state-of-the-art cancer treatment machine

> in the Chili's Care Center (see related story, page 18). The machine, a highly advanced linear accelerator, delivers radiation during cancer treatment. The device combines the ability to image the tumor with the ability to deliver advanced radiation as the instrument moves around the patient. This allows very precise delivery of radiation to the tumor while protecting the child's sensitive tissues.

Schwartz's reasons for giving to St. Jude are twofold. The emotional connection she feels with the staff of St. Jude is important, as is Danny Thomas' vision-one that reflects her desire to help others, a desire that flourished all those years ago during the

Depression.

"I love that this is a place where children are treated equally without regard to their financial status," Schwartz says. "It doesn't matter whether you

are black, white or blue, or whether you are a Christian, Jew or Muslim. St. Jude reflects the kind of world I'd like to see-where there is no hate, and where more people are caring and giving."

To learn more about making a gift to St. Jude or other planned giving opportunities, call ALSAC Gift Planning at (800) 395-1087 or e-mail giftplanning@stjude.org. ●

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Banking on the Future

By Lynda Nance

The Gen H Club is a fun way to teach kids about money management. As they learn the importance of saving, sharing and spending their money, children

money, children gain lifelong skills while helping other kids.



Alissa Campbell Shaw's children, ages 5 and 7, know all the great things that money can buy, but the new St. Jude Generations program teaches them about saving money and helping others, too.

Campbell Shaw, an employee of ALSAC, the fundraising organization of St. Jude, is among the first to participate in this program where parents and grandparents can sign up the children in their lives to be a part of the Gen H Club, which stands for Generation Hope. When children sign up, they receive three-compartment Hopejar[™] Bank kits that separate money for saving, sharing and spending. Along with the kit comes information on how to use each section of the bank.

For Campbell Shaw, using the bank helps reinforce important life lessons.

"My kids are beginning to understand why they need to save money and help others," she says. "We talk about how a

"My kids are beginning to understand why they need to save money and help others."

certain amount of money always needs to be saved, and we work toward saving money to be able to purchase a larger item, even if it's just a Barbie[®] doll for now." She hopes that by teaching her children good money-management skills, they'll not only be financially successful in the future, but also continue to give to others.

And that, says Gloria Peterson, is the idea behind the St. Jude Generations program.

"If we can give people the tools to teach kids about spending, sharing and saving, we can also teach children about St. Jude and how special it is for kids to help other kids," says Peterson, a manager in the National Direct Marketing fundraising program at ALSAC. Kids who begin donating to St. Jude now may well become lifelong St. Jude donors.

Children who sign up for the program receive quarterly newsletters and online access to games and a virtual hospital tour. Sponsors receive two mailings a year, which include activities, such as a blank family tree, that they can complete with the kids in their lives.

When Danny Thomas founded St. Jude in 1962, he kicked off a legacy of family giving that's been passed down to his children, Marlo, Terre and Tony, and his grandchildren. Now, with St. Jude Generations, grandparents and parents can share their own legacy of giving.

To find out more about this special program, call 1-800-730-5084 or visit *www.stjude.org/genhclub.* ●

Three Cheers for Hydroxyurea

Thanks to the research and treatment occurring at St. Jude, more children with sickle cell disease are leading healthy and active lives.



PHOTOS BY ANN-MARGARET HEDGES

For 10-year-old **KRISTIAN HASSELL**, it's become as commonplace as having a glass of orange juice in the morning. But the liquid she drinks each day with her breakfast is far from ordinary.

The liquid is hydroxyurea—a drug therapy used by physicians at St. Jude Children's Research Hospital to treat sickle cell disease.

When Kristian was only 3 weeks old, doctors found that she had sickle cell anemia, the most severe and common form of the disease. By age 4, she was suffering from pain crises, which included bouts of stomach cramps, acute chest syndrome and pneumonia.

"We started taking trips to the hospital every two months and staying about one week at a time," says Kristian's mother, Lisa.

Due to the severity of Kristian's sickle cell anemia, she received a blood transfusion before being referred to St. Jude, where she began undergoing hydroxyurea treatments. Since starting on hydroxyurea in July 2004, Kristian's lifestyle has changed dramatically. The frequent hospital visits are a fading memory.

A daily dose

Russell Ware, MD, PhD, who holds the Lemuel Diggs Endowed Chair of Hematology and chairs the St. Jude Hematology Department, likens taking hydroxyurea to swallowing a powerful vitamin. Hydroxyurea is not a pain medication that relieves aches. Rather, it is a substance that causes the body to produce healthier blood cells.

Sickle cell disease is a blood disorder that causes red blood cells to become hard and sickle-shaped, instead of soft and round. These sickled cells clog blood vessels, depriving organs and tissues of oxygen-carrying blood. Children and adults with the disease may experience symptoms that range from severe pain to strokes, pneumonia, organ damage or death. Hydroxyurea is an effective treatment, as it short-circuits the process of creating the sickle-shaped blood cells.

"When children with sickle cell anemia take hydroxyurea, they make

Russell Ware, MD, PhD, likens taking hydroxyurea to swallowing a powerful vitamin. Hydroxyurea is a substance that causes the body to produce healthier blood cells.



"I'm delighted that Kristian and her family opted for her to start hydroxyurea therapy," says Russell Ware, MD, PhD. "The proof is that now, three years later, she's growing like a regular, healthy child."

blood cells that start out round and stay round," Ware explains.

Hydroxyurea changes the way blood is made so that a child makes blood with less sickle hemoglobin and more fetal hemoglobin, which is a protective form of blood made by all babies at birth. Fetal hemoglobin is lost during the first year of life, Ware says, but hydroxyurea boosts its production to interfere with the sickling process and keep the blood cells round.

Research into the causes and treatment of sickle cell disease began soon after St. Jude opened its doors in 1962. The hospital's first ALSAC grant went to a prominent scientist, Lemuel Diggs, MD, who studied this genetic disorder. Hydroxyurea was administered to children for the first time in the mid-1990s. For the past decade, St. Jude has been a leader in clinical trials that explore the effectiveness of hydroxyurea in children. Once children begin hydroxyurea treatment, they visit St. Jude monthly to check their blood counts. The dose is then adjusted depending on the results until it reaches the maximum tolerated dose. After that, children can move to bimonthly visits, and the dosage is adjusted primarily based on growth and weight gain.

At first, Kristian's parents hesitated to put her on hydroxyurea treatments simply because they didn't know much about the drug. The family discussed the matter thoroughly with Ware and Physician Assistant Nicole Mortier of St. Jude Hematology. A cousin with sickle cell disease also recommended that Kristian take hydroxyurea.

"When I was at St. Jude, everybody was really nice," Kristian says. "I knew they would help me to be stronger."

Kristian began treatment in 2004; in the ensuing years, scientists have learned much more about the drug's capabilities.

"We knew that hydroxyurea, if taken faithfully, given at that maximum tolerated dose, should reduce the number of pain events, pneumonias, hospitalizations, transfusions—all of those acute events that plague children with sickle cell disease," Ware says. "But we have since learned that it also helps protect the internal organs from damage."

Education is key

Since the effects of hydroxyurea cannot be felt or seen immediately, St. Jude Hematology staff allow children to actually see the results by viewing drops of their blood (called blood smears) on glass slides through the lens of a microscope.

"One of the things that we try to do with the kids who are starting hydroxyurea is educate them about the medication and try to get them to understand why they are taking it every day," Mortier says. "That's where looking at the blood smears really helps—taking the kids in to actually show them the changes that it's making because they won't feel the changes right away. They really have to believe that every day that they take it, they're making their blood stronger." Kids view drops of their own blood through the lens of a microscope. "One of the things that we try to do with the kids who are starting hydroxyurea is educate them about the medication and try to get them to understand why they are taking it every day," says Physician Assistant Nicole Mortier.



Nicole Mortier of St. Jude Hematology supervises as Kristian examines a drop of her blood through the microscope. Since the effects of hydroxyurea cannot be felt or seen immediately, children are encouraged to see the results for themselves. The kids can actually see the dramatic decrease in sickled cells by looking through the eyepiece.

Bring it on

After more than three years of taking hydroxyurea daily, Kristian is now participating in activities that her parents thought were impossible when she arrived at St. Jude.

"This is the first year I really felt comfortable letting her get into something because she would get tired really fast," Lisa says.

Kristian enjoys playing basketball and volleyball, but cheerleading takes up most of her recreational time. Her competitive squad spends evenings and Saturday mornings preparing for competition. Kristian serves as a base for stunts, which involves holding and tossing another squad member in the air.

"I like to call the cheers," she says, "but we have to exercise a lot and run a lot of laps."

The amount of physical activity concerned Lisa at first, but Kristian has met the task with a new, energetic attitude that was not present during her younger years. Kristian also likes to show off her latest cheers to anyone who will watch.

"She did a cheer for us at her last clinic visit," Mortier says. "She's always on the move."

Do the HUSTLE

Kristian visits St. Jude every eight weeks to have her blood counts monitored. A special scan is performed periodically to check her spleen function, which has improved since beginning hydroxyurea treatment.

"She has very few circulating sickle cells at this point, which is exciting for her to see," Mortier says. "She's one of the shining examples of children who have done well on hydroxyurea, but her story is not unique."

From a research perspective, Kristian is a high responder to treatment, Ware says. As a result, she is involved in a St. Jude research protocol titled HUSTLE that investigates why some children respond better than others to the drug.

"We're looking at how it works and all of the drug's effects, both good and bad," Ware says of the study, which is an acronym for hydroxyurea (HU) study (ST) of late effects (LE).

Nearly 150 or one-third of St. Jude children with sickle cell anemia are currently taking hydroxyurea, Ware says. Clinical protocols are in place that will put more children on the medication, particularly younger children.

HUSTLE is one of several research protocols for sickle cell disease at St. Jude, which is also leading a national trial in infants to determine hydroxyurea's ability to limit organ damage.

"I'm delighted that Kristian and her family opted for her to start hydroxyurea therapy," Ware says. "The proof is that now, three years later, she's growing like a regular, healthy child."●

Putting the BRAKES on the Immune System



Dario Vignali, PhD, of St. Jude Immunology and Lauren Collison, PhD, a postdoctoral fellow in Vignali's laboratory, purify proteins. They discovered an important signaling molecule that could have applications for fighting cancer, as well as for a host of autoimmune and inflammatory diseases, including type 1 diabetes, multiple sclerosis, Crohn's disease and asthma.

St. Jude scientists discover a signaling molecule that puts a stop to runaway immune responses.

By Elizabeth Jane Walker

s any sports autom is just

s any aficionado of exotic sports cars can attest, an automobile's brake system is just as crucial as its

acceleration potential. After all, a Ferrari hurtling along at 205 miles per hour needs an extremely effective braking system. Similarly, scientists at St. Jude Children's Research Hospital have discovered an important signaling molecule that puts the brakes on a rogue immune response. The discovery could have applications for a host of autoimmune and inflammatory diseases, including type 1 diabetes, multiple sclerosis, Crohn's disease and asthma. The finding could also have exciting ramifications for fighting cancer.

T cells are a type of white blood cell that play an important role in the body's immune response. Different kinds of T cells have drastically different functions. "Effector T cells mediate immune responses, like accelerators make cars go forward, while a specialized population called regulatory T cells stop an immune response like brakes slow down a car," says Dario Vignali, PhD, of St. Jude Immunology. Created in the thymus, a T cell (or T lymphocyte) is a type of white blood cell that helps protect the body against infection and disease. Effector T cells initiate and orchestrate the immune response. Regulatory T cells suppress or stop an immune response.

"Regulatory T cells actively suppress the activation of effector T cells that are reactive and damaging to self tissues, thereby preventing autoimmune disease." explains Lauren Collison, PhD, a postdoctoral fellow in Vignali's laboratory. "In the context of an infection, after the effector T cell has orchestrated the correct immune response and the pathogen is gone, regulatory T cells can help calm down the immune system."

Vignali, Collison and their colleagues recently discovered that regulatory T cells release a protein complex called interleukin-35 (IL-35), which consists of two proteins. IL-35 is a cytokine, a chemical messenger protein that helps cells communicate with one another. The researchers also discovered that IL-35 acts as a brake on the aggressive effector T cells, a finding that, like a Ferrari itself, puts this cytokine in a class of its own.

Scientists have identified more than 40 cytokines. Some act as accelerators; others as brakes. "The vast majority of cytokines are 'go' signals," Vignali says. "In contrast, there are very few that issue 'stop' signals—only two or three—so IL-35 is special.""

In fact, IL-35 is the only known cytokine that is made specifically by regulatory T cells and can directly suppress the activity of effector T cells.

"This discovery adds significantly to our understanding of how these cells prevent immune responses from running out of control and causing damage," Vignali says. "To return to the car analogy, IL-35 may turn out to be a very important brake for the immune system."

Forward and reverse

St. Jude immunologists look for ways to treat infections, cancer and other diseases by manipulating the immune system. People develop autoimmune diseases when the immune system "Experimental studies have shown that if you can remove regulatory T cells or dampen their activity, then tumor immunity becomes vigorous, and the body can get rid of the tumor."

becomes overactive. Evidence indicates that regulatory T cells are partially defective in a variety of these diseases. Vignali says novel treatments that add IL-35 or boost IL-35 activity may provide new therapeutic opportunities for autoimmune disorders by putting the brakes on the destructive attacks of the immune system. Such treatments may also help in inflammatory conditions such as asthma.

The situation may be reversed in many cancers. "There is mounting evidence that regulatory T cells stop our ability to eradicate tumors," Vignali explains. "Tumors produce a dilemma within the immune system: On one hand, the system wants to get rid of the tumor cells, but on the other hand, they're a part of us. Thus, regulatory T cells may prevent the immune system from attacking the tumor. Experimental studies have shown that if you can remove regulatory T cells or dampen their activity, then tumor immunity becomes vigorous, and the body can get rid of the tumor."

A number of ongoing preclinical studies and clinical trials are studying

drugs that block regulatory T cells, according to Vignali. These "brake" drugs could be combined with cancer vaccines to produce more effective therapies for certain types of cancer that can't be treated by conventional approaches, such as chemotherapy and radiation. Cancer vaccines stimulate the immune system to recognize and attack specific targets, such as germs or cancer cells.

"Regulatory T cells are seen as a major impediment to the development of effective anti-cancer vaccines and may prevent sterilizing immunity in certain chronic infections, such as hepatitis C and tuberculosis," Vignali says. "Blocking the activity of IL-35 may reduce the function of regulatory T cells and their ability to block anti-tumor immune responses. So treatments that block IL-35 activity may make anti-cancer vaccines more effective."

Accelerating science

The discovery of IL-35 was chronicled in the November 2007 issue of the journal *Nature*. That's a heady accomplishment for a young scientist like Collison, who arrived in Vignali's lab less than two years ago.

"When I interviewed with Dario, he said the best thing about St. Jude is that your only limitation is your imagination, and he was right," she says. "One of the best things about science is the fact that your discovery attracts the interest of other bright minds. Other scientists will hear about IL-35 and say, 'Maybe this new protein is important in the disease process or condition that I'm studying.' By collaborating with others whose expertise is different than ours, we can hasten progress."

Collison is careful to keep her eyes on the ultimate goal: cures for children with cancer and other catastrophic diseases. "I believe this protein has a good chance of having therapeutic applications," Collison says. "I'm a St. Jude donor myself, and like other donors, I think it's important to remember that at the end of the day the goal of our research is to treat patients—especially the children we have here at St. Jude."●

St. Jude on the Double

Of the more than 1,000 transplants performed at St. Jude, Kara Lee's will be the fourth to use stem cells from an identical twin, and the first time an identical twin donor is used to treat neuroblastoma.

By Summer Freeman

More than four years ago, Megan Lee surprised her husband, Tony, with a small, modest package. Unwrapped, the present revealed exceptional news. A pair of baby shoes, delicate and tiny, both fitting easily in just one of Tony's hands, announced the impending arrival of their third child. Weeks later, a doctor's visit held another surprise—the couple needed to invest in a second pair of shoes.

The news was welcomed, but the idea of the family growing from four to six so quickly was a bit intimidating, Megan remembers. "The day I went in for delivery, I sat there in the room, staring at two little beds and two little piles of diapers and thought, 'I'm so overwhelmed." She laughs at the thought today, knowing that the news of two now holds a second chance for one.

As Megan recounts the events that led her to St. Jude Children's Research Hospital, her eyes, a serene blue, reflect a quiet strength. That same shade of blue is repeated in the eyes of her identical twins, Kara and Lauren, who play nearby.

At first glance, many people would wince at the family's situation. Four-year-old Kara is battling stage IV neuroblastoma, an advanced form of the cancer that arises from the sympathetic nervous system, which runs from the base of the neck to the tailbone. Most daunting, the disease that has invaded Kara's small body is aggressive and persistent.

Double take

Aside from the support of family and friends, care from hospital staff and a shared camaraderie among St. Jude parents who are all facing similar struggles, Megan finds comfort in the precious fact that Lauren is the best possible donor match for the stem cell transplant needed to treat Kara's cancer.

"One of the nurses joked with me, 'Now you know why you have two,"" Megan says. "I think Lauren will one day have a great sense of pride knowing that she was able to help her sister this way."

As sisters, Lauren and Kara are close; as twins, they share a unique bond. Older by one minute, Lauren was as reserved and contemplative as Kara was boisterous and outgoing. It was the change in Kara's temperament that hinted at larger problems.

"Kara grew quiet," Megan says. "At first, it seemed like she had a cold. She was achy and limping and had a low-grade temperature. Her color was off. Things come to your mind when you're at home trying to figure out what could be wrong with your child, but cancer isn't one of them."

A local nurse practitioner diagnosed

an upper-respiratory infection and prescribed antibiotics. When the drugs had run their course and the fever persisted, the family checked into a children's hospital outside of their hometown. Doctors conducted a string of tests. "They said something was wrong with her blood, and they wanted to keep her overnight," Megan remembers. "They told us it could be a number of things, including cancer, but they weren't sure." Within days, the stage IV neuroblastoma diagnosis was made.

Matching gifts

The Lees took in the news. "To be told that about your little girl, it felt like someone ripped my heart out," Tony recalls. "It was such a helpless feeling. I told my wife that day, 'I want to go to St. Jude if we can." While Tony had never been to St. Jude, a family in the Lees' church had a son treated at the hospital a few years ago. "I knew what St. Jude had done for him, and of course, wanted the best for Kara," Tony says.

While Tony was settled, Megan wrestled with the idea of her family being separated. Going to St. Jude would necessitate leaving the Lees' two oldest children, Erica, 9, and Brent, 7, behind with relatives. "It was hard to think about the family being separated," Megan says,



Kara Lee (foreground) owes her life to the physicians and researchers at St. Jude—and to her identical twin sister, Lauren, who will serve as her bone marrow donor.

"It felt like someone ripped my heart out. It was such a helpless feeling. I told my wife that day, 'I want to go to St. Jude if we can.""



"but we didn't have medical insurance at the time and St. Jude doesn't turn anyone away if they can't pay." Another benefit to St. Jude was that Kara's care could be done in one place. "Had we stayed at home, her chemo, her transplant and her radiation treatments would have had to be done at different places," Megan says.

The doctor at their hometown hospital supported the family's decision to take Kara to Memphis. "He knew some of the doctors at St. Jude and said that he would do everything that he could if that is where we wanted to be," Tony says.

In early June 2007, three days after the diagnosis, the Lees arrived at St. Jude, where they soon met Kara's oncologist, Wayne Furman, MD, and her surgeon, Andrew Davidoff, MD. Kara underwent chemotherapy and was scheduled for an operation in mid-August to remove the primary tumor in her adrenal gland. The day before Kara's surgery, the Lees learned the tumor was wrapped around her aorta.

"It's common for high-risk neuroblastoma," says Davidoff, division chief of St. Jude General Pediatric Surgery. "Knowing that, we planned to be in the operating room all day." During the eight-hour procedure, Davidoff and his team removed the primary tumor, in addition to numerous adjacent lymph nodes containing tumor.

After the operation, Kara continued

Kara charms her oncologist, Wayne Furman, MD, with a shy smile.

chemotherapy and was scheduled for an autologous stem cell transplant in early November. In this type of transplant, bone marrow stem cells are collected from the patients and later given back after the hematopoietic (blood stem cell) system is cleared of cancer. Because Kara and Lauren are identical twins and share the same DNA, doctors opted to use Lauren as the transplant donor.

"It is like giving Kara her own marrow back but only healthier," says Sandy Kovach, a St. Jude nurse practitioner. "It gives Kara the better option."

Twin win

Before Kara's illness, the Lees did not know the twins were identical. Testing conducted at their birth yielded inclusive results. When doctors outlined Kara's treatment plan at St. Jude, they tested Lauren's blood in hopes that it would be an identical match.

In general, patients only have a 25 to 30 percent chance of having a sibling who is an HLA-match, and the chance of having an identical twin is drastically lower. HLA testing is a scan of human leukocyte antigens found in blood that determines if a potential donor is a suitable match for the person in need of a transplant.

Megan says she is thankful that God gave Kara a twin, providing a perfect match. "We look at it as a gift," she says. "It is truly a blessing."

Of the more than 1,000 transplants performed at St. Jude, Kara's will be the fourth to use stem cells from an identical twin. It will also be the first time an identical twin donor is used to treat neuroblastoma, since previous St. Jude transplants involving identical twins were for lymphomas and leukemias.

In November, doctors decided to postpone the procedure until more of Kara's marrow is cleared of disease. "We need to give a few extra courses (of chemotherapy) to make sure we've got the marrow disease as far down as we can get it," Kovach says. "It's more aggressive treatment, and extending therapy longer makes sure Kara has the best chance."

While Kara undergoes treatment, Megan and Lauren stay with her in St. Jude housing. Tony and the girls' grandparents take turns staying with them as well. Like all siblings in close quarters, the twins squabble, but reconcile quickly and are each other's favorite playmate.

In an unusual twist, Megan says the girls have swapped temperaments during their time at the hospital. "Lauren was always shy, and Kara was energetic, but now it seems like they've reversed roles," she says. Part of Lauren's new role is as nurturing big sister. "It's hard for them—just being 4 years old—to grasp everything that is going on, but Lauren knows that she is going to help Kara," Megan says.

But sometimes even big sisters need a break. "Lauren told her grandmother the other day, 'Somebody's going to have to help Kara for a while; I'm too tired," Megan says, laughing.

Through her faith, Megan has found calm in the chaos. "With God, we are not alone in this fight," she says. "I don't know why this has to happen to Kara, but I know this is where we should be."

The experience, although grueling at times, has produced special moments between the two sisters, strengthening their connection for a lifetime.

"Sometimes I'll catch them just sitting, tangled in a hug," Tony says. "It's such a good feeling." ●



Coming to the Table for Discovery

The department of Chemical Biology and Therapeutics brings discoveries from the bench to the bedside—creating new therapies for catastrophic pediatric diseases. henever family and friends are invited to your home, chances are the evening will end with everyone lingering in the kitchen. Perhaps someone has a warm pot of coffee to share, a story or a

hearty laugh. Whatever the attraction, the heart of the home beats strongest when everyone joins together. At St. Jude Children's Research Hospital, the Chemical Biology and Therapeutics (CBT) department serves a similar role. If the basic research and clinical research areas of the hospital were cousins from different sides of the family, CBT is where they would come together to break bread and, more importantly, to create new recipes for more effective and less-toxic treatments for catastrophic pediatric illnesses.

The head chef of the operation is Kip Guy, PhD, department chair, and the main dish is drug discovery. But Guy is not a knife-wielding, spotlight-stealing, celebrity-type gourmand. In his arena, too many chefs don't spoil the broth—they all contribute something to the mix.

A key ingredient

"In our department we work with numerous people across the hospital from a basic researcher in the lab to clinicians who are interested in taking new drugs to the clinic. These are extremely complex and multidisciplinary projects," Guy says. "The only way these collaborations work functionally is when groups of highly skilled people come



Kip Guy, PhD, Chemical Biology and Therapeutics chair, brings clinicians and researchers together to create new drugs that may save the lives of children.

"Walking into our department is like finding a small, biotech company within the confines of a research hospital."

together, each bringing an individual expertise."

So what does CBT bring to the table?

"We are the crucial link in the translational research process," says Julianne Bryan, CBT director of operations. "We help bridge the gap between basic research and clinical research—from the bench to the bedside. Our department facilitates the teamwork necessary to pursue drug discovery projects and supports the process with the chemistry skills needed to ultimately deliver therapies to children in the clinic."

This focus on therapy and treatment was one of the primary elements that drew Guy to St. Jude in the spring of 2005 to establish the department.

"Initially it was being called a department of Chemical Biology [the study of biology using chemical tools], but I said, 'That's not really what I'm interested in doing,'" Guy explains. "I suggested it should be called the department of Chemical Biology and *Therapeutics* and that its goal should be to discover new treatments rather than focusing strictly on academic pursuits."

The other magnetic force was the hospital's mission. "That was a major difference from other research hospitals, and it's what really brought me here," Guy says.

Find, make, refine

The origins of those applications begin at the molecular level. Just as the kitchen is the center of the home, small molecules are at the core of almost everything CBT does. Guy explains that the primary focus of the department is to find small molecules that share characteristics with drugs, even though they are not yet proven to have therapeutic utility, and to explore how they affect disease processes.

This is achieved through a complex, high-throughput screening process in which literally hundreds of thousands of new and existing compounds are tested for their effect on specific molecular targets that drive disease.

In the instance of cancer, when a cell is mutated and receives a message to multiply uncontrollably, this testing enables CBT to pose the question, "Can we revert this mutation by the application of this compound in such a way that it will cause a tumor to shrink or be destroyed?"

Once a reaction or "hit" has been identified or found in the screening process, things are just starting to cook. The CBT faculty and staff must perform their molecular magic, making the compound potent and selective enough to show promise for human use. Then these compounds must be refined even further before testing can begin at the clinical level.

Coming to the table

"The amount of work in producing a pre-clinical candidate is incredible. It entails five to seven years of work involving groups of 15 to 20 people from all different disciplines," Guy explains. "It's a lot of expertise to bring together in one institution. It's absolutely unique."

CBT is participating in numerous collaborative studies across the hospital; however, some pursuits reach beyond the walls of St. Jude. One such project involves Richard Gilbertson, MD, PhD, co-leader of the Neurobiology and Brain Tumor Program. He is spearheading a project between the St. Jude department of Developmental Neurobiology and The University of Texas M. D. Anderson Cancer Center in Houston.

"We have formed the first, direct collaboration between pediatric and adult oncologists to tackle ependymoma, a brain tumor that affects both children and adults," Gilbertson explains. "Before CBT came on board, we were totally dependent on large pharmaceutical companies to make a drug or compound that might target this disease. In reality, unless there was one already available, you could forget it. Thanks to CBT, we can actually do that work ourselves and be directly involved in the earliest stages of drug development."

Guy explains that drug production for

childhood diseases is not economically feasible for large pharmaceutical companies.

"We are not trying to compete with drug manufacturers; we hope to partner with them," Guy says. "The more we can do on our end to reduce risk of failure when we move compounds to the clinical level, the more likely the pharmaceutical companies will be interested in taking on our projects and doing the final stages of production so we can get these treatments to the children who need them."

Similar screening is conducted in academic settings across the country, but Guy cites two factors that set the St. Jude approach apart from others: first, the tremendous efforts taken to screen the *right* materials when researching pediatric diseases, followed by the focus on creating functional, useful molecules with practical, clinical applications.

Recipe for success

Of course, any recipe for success calls for the appropriate blend of

manpower, ingredients and utensils.

"The fact that we have this tremendous facility with the right people and the right equipment says that St. Jude is serious about drug discovery," observes Bryan. "Walking into our department is like finding a small, biotech company within the confines of a research hospital."

Particularly impressive is the department's state-of-the-art, compound storage system called the REMP Mid-Sized Store[®]. The REMP can hold up to 11 million vials of chemical compounds at a constant, subfreezing temperature, thus protecting the delicate molecules from damaging freeze-thaw cycles while maintaining the integrity and shelf life of the other stored compounds. This unit is one of four CBT robotic devices that have helped put St. Jude on the drug discovery map.

Despite the excitement surrounding these technological marvels, Guy is quick to put the high-tech tools into perspective. "People see the robots, and they think they're pretty snazzy but they don't often grasp the idea that the robots are part of a workflow," Guy says. "It's the people, the materials *and* the equipment; you need all of those things working together in a coherent system in order to be successful at this work."

Icing on the cake

Gilbertson, who has been with St. Jude for seven years, enjoys the camaraderie and teamwork fostered by the CBT department's approach to research.

"Kip Guy's group brings a unique science to St. Jude with different techniques and technologies. It's like making a cake—it's a new ingredient that takes something that was good before and makes it truly great, an extra spice that flavors the way you approach your work," Gilbertson says. "As a researcher, it would be difficult to envision how St. Jude could move to the next level in its mission without CBT." ●



Alexander Arnold, PhD, of Chemical Biology and Therapeutics, and Jennifer Atkinson, PhD, of Developmental Neurobiology, discuss a research project that uses one of the hospital's robots for drug discovery. St. Jude children named the four robots used by Chemical Biology and Therapeutics; the robot in this cubicle is named Billy the Robot; another one in the same room is named Tobor, which is "robot" spelled backwards.

Turning Scientific Beliefs Upside-down

St. Jude investigators disprove a century-old theory, turning established scientific beliefs on their heads. This exciting discovery may someday have applications for such diseases as Alzheimer's and Parkinson's.



Stanislav Zakharenko, MD, PhD (foreground), and Ildar Bayazitov, PhD, both of Developmental Neurobiology, examine images on the monitor of a two-photon microscope. Because of their work in the microscopy lab, St. Jude researchers were able to see neurons divide in real time.

By Mike O'Kelly

R ecently, a century's worth of ingrained scientific belief was turned upside-down. Just like *that*.

Nobody questioned one of the longstanding principles in the field of developmental neurobiology—until a team from St. Jude Children's Research Hospital disproved it as part of a project to study a completely different topic.

For more than 100 years, scientists had assumed that neurons in the brain are permanent and cannot divide to produce new neurons. But while studying the genes that contribute to retinoblastoma, Michael Dyer, PhD, and his colleagues were able to coax neurons to make more neurons for the first time. Their discovery disproves the scientific theory that differentiated (or mature) nerves cannot multiply.

"One of the most exciting things about research is when you are studying one question and come across a completely unexpected discovery that has a much broader impact," says Dyer, of St. Jude Developmental Neurobiology.

Analyzing the facts

Dyer and his colleagues are now analyzing their discovery to figure out

why the particular neuron they studied multiplied, whether other neurons can react similarly and if neurons can be

manipulated to repeat the same action. If differentiated neurons can be altered so that they temporarily multiply, it could create new treatments for neurodegenerative diseases such as Alzheimer's and Parkinson's.

Dyer says this treatment of existing nerves

duplicating themselves might be more efficient than inserting stem cells into the brain in an attempt to regenerate lost neurons.

An image of the dividing

microscope.

neuron as seen through the

"There is still a lot of research required to determine if it is possible to control gene activity to make this approach practical," Dyer explains.

The discovery also challenges the belief that cancer cells are most aggressive when they are undifferentiated. During the differentiation process, cells lose their primitive, stem-cell–like properties, which include the ability to grow and multiply, and instead develop specialized shapes and functions.

Dyer says that cancer cells in such diseases as chronic myelogeneous leukemia are less aggressive when they are differentiated.

The opposite result was discovered in Dyer's recent research on retinoblastoma.

"In the model that we were studying, these dividing neurons eventually become tumors, and they go on to form retinoblastoma," Dyer explains. "The tumors look quite differentiated. They have processes and synapses, and they look like neurons. I would



"St. Jude state-ofthe-art resources for research on catastrophic childhood illness made this finding possible."



Michael Dyer, PhD (at left), of St. Jude Developmental Neurobiology collaborates with postdoctoral fellow Itsuki Ajioka, PhD. Their team made an astounding discovery when Ajioka noticed nerves that seemed to be dividing. The discovery disproves the scientific theory that mature nerves cannot multiply.

have predicted, based on this cancer model, that they'd be mild tumors, not aggressive. It turns out that it's exactly the opposite—they're the most aggressive tumors we've ever seen in our model.

"This really challenges the idea that differentiated means less aggressive and undifferentiated means aggressive."

Surprising results

This development is also important because it could change therapies not only for retinoblastoma but for other tumors where differentiation is induced with the intent of making cells less aggressive.

The discovery was first reported to Dyer by postdoctoral fellow Itsuki Ajioka, PhD, when Ajioka noticed an increase in the number of nerves in the retina called horizontal interneurons. These specialized neurons were mature and were considered incapable of dividing. When the investigators allowed this cell division to continue, highly differentiated tumors formed that resembled normal horizontal interneurons.

Since the results were so surprising, Dyer says it took 18 months for the team to confirm the finding by making sure that the nerve cells themselves were dividing and verifying that the increase was not due to a previously undiscovered immature cell.

Stanislav Zakharenko, MD, PhD, of Developmental Neurobiology heads

the lab that performed the project's microscopy studies.

"The state-of-the-art resources for research on catastrophic childhood illness made this finding possible," Dyer said. "St. Jude has some of the world's leaders in cutting-edge microscopy to visualize neurons and tumors such as our collaborator on the study, Dr. Stanislav Zakharenko."

The advanced microscopy services at St. Jude played an important part in this research, as investigators watched the neurons divide in real time with technology not available as recently as a few years ago.

"There's nothing like seeing it happen," Dyer says. "Without that technology, we would not have been able to do what we did or to prove it in that kind of definitive way."

Future possibilities

The team's discovery could lead to the development of new therapies to treat retinoblastoma that has spread to other parts of the body. Such treatment could result from understanding why differentiated tumors that resemble neurons are aggressive and metastasize, or spread, to the brain, bone marrow and lymph nodes.

Additional research is necessary to see if these findings could lead to new treatments for diseases such as Alzheimer's and Parkinson's neurodegenerative disorders that occur when differentiated nerves in the brain try to multiply, but instead undergo cell death, a process called apoptosis.

If researchers can alter the activity of certain genes in differentiated neurons, they might be able to trigger them to multiply temporarily and replace the neighboring neurons that were lost as a result of the disorder.

"The next step in this research is to determine if we can extend these findings to other types of neurons in the retina and brain," Dyer says. "If we can induce a variety of neuronal types to divide, then our discovery may have much broader implications for treating neurodegeneration." ●

Chili's Care Center: Under One Roof

The Chili's Care Center brings clinicians and scientists together to find cures and save children.

By Carrie L. Strehlau



n 2004, when construction began on the Chili's Care Center, the building was only a vision on paper. It took hundreds of people to turn that vision into reality for the patients, researchers, clinicians and staff of St. Jude Children's Research Hospital. November 2007 welcomed the magnificent building to the St. Jude campus.

"The Chili's Care Center is a significant part of our long-term strategy to translate basic research at St. Jude into the most advanced and effective care of patients," says William E. Evans, PharmD, St. Jude director and CEO.

Named to honor Chili's Grill & Bar's close partnership with St. Jude, the Chili's Care Center combines 21st century imaging and treatment technology with the hospital's almost half-century approach to medicine. Historically, St. Jude has placed patients and scientists in proximity to fasttrack the translation of new knowledge into improved and more effective care. This bench-to-bedside model is reflected in the Chili's Care Center, where patient rooms and procedure areas are located in the same building as research labs. The configuration helps speed medical outcomes, positioning St. Jude as a leading institution that is changing boundaries in the world of research and patient care.

"Integrating patient care and research holds the key to more rapid advances in science and medicine," Evans says. "This new facility will help us maintain our leadership role in defining the forefront of research to advance the treatment of children with cancer and other catastrophic pediatric diseases."

Enhancing research and treatment

The six-story, 340,000-squarefoot building will hold the hospital's Radiological Sciences department; new, larger research laboratories for Pharmaceutical Sciences, Pathology and Virology; an 18-bed Bone Marrow Transplant inpatient unit with expanded patient and parent suites; and academic offices for faculty and staff.

The main motivation for constructing the Chili's Care Center, however, was the need to expand and modernize facilities for the Radiological Sciences department, including Diagnostic Imaging and Radiation Oncology. The patient care areas in this department had not been renovated since construction of the initial 1962 and 1975 buildings.

"The new facilities in the Chili's Care



Facing page: Julie Smith of Radiological Sciences and department chair Larry Kun, MD, prepare for patients in the Radiological Sciences area of the new facility. The patient care areas of the building feature bright colors, engaging artwork and countertops built at a child's-eye level. PHOTOS BY SETH DIXON

Above: Scott Snyder, PhD, of Radiological Sciences, explains the function of the hospital's cyclotron. This state-of-the-art machine will provide an array of new research initiatives in nuclear chemistry and nuclear medicine. PHOTO BY GAELLE LLAMBI

Center provide opportunity to greatly enhance our diagnostic capabilities in X-ray, nuclear medicine, CT and MRI in addition to providing a state-of-the-art suite for interventional radiology," says Larry Kun, MD, Radiological Sciences chair.

"The provision of new space for Radiation Oncology allows us to introduce new technology to better localize and accurately target tumors, while adding capabilities in high doserate brachytherapy (a procedure in which radioactive source is placed inside or next to the tumor). These radioactive implants are not often used in other centers for childhood cancer."

Past, present, future

Eight exam and consultation rooms double what the hospital had—provide ample space for routine patient exams and for the patient care team, patients and families to discuss treatment options. The new area for radiation also has an infusion room, private changing area, its own Child Life room, as well as CT/CT PET, MRI, X-ray and sonogram machines.

"The building has three linear accelerator vaults, which have 4-to-8foot-thick walls for radiation shielding purposes," says John Curran, Design and Construction department director. "The ceiling in there is 10-and-a-half feet thick." Linear accelerators will be used to provide radiation therapy for children with cancer.

"The MRIs in the building are also unique in that there is a floor below and patient rooms above," Curran says. "As far as I know, this is the first time in the world for this configuration."

To insulate patient rooms from the vibrations and sounds of the MRIs, three ceilings were built between the floors. An acoustic engineering consultant was brought in to ensure there was enough sound dampening between the two floors.

The Radiation Oncology division will use sophisticated 3-D imaging and linear accelerator technologies to produce highly conformal treatment plans.

New horizons

A new addition to the St. Jude campus is the cyclotron. This state-ofthe-art machine will provide opportunities for an array of new research initiatives in nuclear chemistry and nuclear medicine. Scientists will be able to use novel radiolabeled pharmaceuticals to track tumor extent and response to therapies.

"This is the only cyclotron dedicated to producing tracers solely for understanding and developing treatments for catastrophic childhood diseases," says Barry Shulkin, MD, Nuclear Medicine division chief.

"The cyclotron and associated nuclear chemistry lab give St. Jude the opportunity to begin a program in molecular imaging research, to provide novel diagnostic tools and move toward new therapeutic approaches for some of the more common, less successfully treated brain tumors and solid tumors in children," Kun says. "Using short-lived radioactive tracers, we are going to be able to target specific tumor types or areas of tumor activity that should allow us to better identify areas of tumor involvement and responses associated with therapy."

The Chili's Care Center houses technological resources that will allow an entirely new area of diagnostic investigation to take place. The advanced technology in the building makes it possible to create radioisotopes on site. Radioisotopes that only last several minutes to a few hours can be quickly combined with an antibody or a compound that will bind to and identify a tumor. "Ultimately, one can easily envision producing radioactive antibodies or chemicals that aid in targeted therapy, as well," Kun says.

Focus on families

Walkways reaching out from the hospital will bring patients and employees into the building where clinicians and scientists will do research that promises to increase the survival rates of catastrophic pediatric diseases.

The functionality of the Chili's Care Center design is due to St. Jude parents, who served as assistant interior designers by offering their input through



St. Jude patient Katie Griffin marvels at marine life in the Chili's Care Center 850-gallon saltwater living coral tank.

focus groups, and to the numerous staff who guided the design of the building to ensure it would have a welcoming atmosphere and friendly interior.

From the color of the walls to the countertops built at a child's eye-level to the 850-gallon saltwater living coral tank in the lobby, the Chili's Care Center is designed to be a unique, child-friendly place. Important to this project is the original artwork that patients provided to hang alongside unique works from St. Jude photographers and local artists.

"It is a large, beautiful collection,"

says Claudio Perez-Leon, the Memphisbased artist who coordinated the artwork and artists for the building. "Some of the artwork is playful and abstract. Others are figurative. Others are more like fantasies that you would find in a children's book. Others are biographical. We wanted to do something whimsical that would uplift people."

Continuing the dream of St. Jude founder Danny Thomas, the Chili's Care Center is a true representation of the future of St. Jude and its dedication to finding cures and saving children.

Facts about the Chili's Care Center

- » The foundation of the Chili's Care Center was the largest concrete pour in Memphis history. It took more than 15 hours to deliver the nearly 900 truck loads of concrete.
- » Between each floor is an extra floor. This allows for repair work to be done over a patient room or laboratory without the patient or staff evacuating the building or having health or research compromised.
- » Each research laboratory in the Chili's Care Center is approximately 725 square feet. The addition of these new laboratories brings the total campus lab count to 182.
- » The first floor lobby overlooks the plaza level lobby. In addition to the glass wall that surrounds the lobby, there is a 40-foot blue waterfall glass design element with a small, circular glass floor.
- » The patient rooms—called patient suites—are a third larger than existing patient rooms in the St. Jude Patient Care Center, and the parent rooms are three times bigger than existing parent rooms.
- » The spacious patient suites were designed to offer sweeping views of the hospital campus.

Beauty in the Beast

BY ELIZABETH JANE WALKER

hey call him "the Beast." That's an ominous nickname for a turbo-charged 2-year-old with a cherubic countenance and an engaging smile. But as Sam Gillott's parents chase their son from place to place, they revel in the aspects of his character that inspired that moniker—Sam's kinetic energy, his quick intelligence, his headstrong attitude, his fighting spirit.

"He's so strong and so vibrant," says his mom. "He's a beast who looks like an angel. Sam's a child of extremes. He can be frustrated and irritable like any toddler. But when he's happy and playing, I'd bottle it up and hold him forever."

Brian and Lisa Gillott constantly make new discoveries about their son's character, as he develops definite opinions and responds to new experiences. These days, trucks and trains elicit excitement; naptime prompts an outburst of temper as violent and ephemeral as a summer storm. But other people are learning from Sam, as well. This tiny boy is helping scientists at St. Jude Children's Research Hospital uncover crucial information about the interplay of two devastating diseases—a rare form of Fanconi anemia and a malignant brain tumor called medulloblastoma. The knowledge gained may one day help other children who suffer from the same illnesses.

Because of one spirited toddler, scientists are learning more about a rare disorder lessons that may benefit many other children in the coming years.

Sam Gillott zips down the slide at Target House. This high-energy toddler is helping scientists at St. Jude uncover crucial information about the interplay of two devastating diseases.

"For us, St. Jude was like a light in the dark."

Déjà vu

Look into the eyes of Sam's parents and you'll see maturity born of heartbreak, fatigue spawned by stress...and hope that endures in spite of adversity. You'll see a young couple who have traveled this road before.

Nearly four years ago, their firstborn son, Ben, was found to have a malignant brain tumor. The 13-month-old underwent chemotherapy at a hospital near their home in New York. The aggressive treatment provoked one complication after another. After only three months, Brian and Lisa lost their beautiful child. In addition to dealing with overwhelming grief, they also discovered that they owed \$400,000 in medical bills. "What do you do with that?" Lisa asks. "We'd just lost our son. It was terrible."

Physicians assured the couple that the cancer was an isolated incident, and that they could have other children. Four months after Ben's death, Lisa became pregnant again—news that provided a glimmer of sunlight in a dark landscape of grief. "Honestly, Sam is what got me through it," she says.

Lisa and Brian saw glimpses of Ben in their newborn son. Sam had his brother's smile, the same infectious laugh. But the similarities stopped there. "Ben was more mellow, more laid back," Lisa muses. "Sam is 'go, go, go.' He's much more aggressive, a fighter. This kid started walking at 14 months and has been running ever since."

In May of 2007, Sam developed an ear infection and began tilting his head to the left. A round of antibiotics cleared up the infection, but the perplexing symptoms escalated. The pediatrician instructed the Gillotts to take Sam to the hospital in New York where Ben had died. Walking into that building took all of the courage the couple could muster.

"This is the hospital that I had lived in for almost three months," Lisa says. "I had walked in with Ben, and I had walked out without him. I couldn't even drive down that street without cringing. But I didn't have a choice."

After a battery of tests, the doctors told Lisa and Brian that Sam had a brain tumor.

"I beat up a room; tore stuff off the walls," Lisa admits. "I watched my husband collapse. I watched my mother



Legs too short to reach the pedals? No problem! Brian offers his son a helping hand. Lisa says that's just what St. Jude has done for Sam, as well, by offering the family world-class treatment, compassion and hope. "Everybody in this place eats, sleeps and breathes these kids and the hope of getting them through one more day, through one more week, through forever," she says.

age 10 years in two seconds. And I looked at my child and said, 'How is this possible? How is this happening again?'"

A light in the dark

The couple immediately contacted pediatric oncologists in their region. "If we came to you, what would your treatment plan be?" they asked. Most

> physicians wanted to use a variation of the protocol that had been used on Ben. "But that treatment killed our son," the Gillotts challenged. "How can you just go forth with the same plan?"

That approach to treatment was simply unacceptable to Lisa and Brian.

Lisa remembered that her mother and grandfather had donated to St. Jude for many years, so she expanded her search by logging onto the hospital's Web site. She e-mailed the hospital's brain tumor program. Within an hour, she received a phone call from St. Jude neurooncologist Robert Sanders, MD. "He spent more than two hours on the phone with me on a Saturday," Lisa says. "That Sunday he spent another hour on the phone with me. Memorial Day, I e-mailed him with a question. Even though he was with his family on vacation, he called to talk to me."

Brian and Lisa liked what they heard. "Dr. Sanders was totally aware of the toxicity issues and understood that, yes, you have to be aggressive—after all, it's cancer," Lisa said. "But you have to balance that aggressiveness with the least toxicity, providing the best quality of life while you're undergoing treatment."

"Our philosophy has been to use treatment that is less intense than the treatments many people are doing in the rest of the country," Sanders explains. "So it worked out nicely that what we were doing was what Lisa was looking for."

"For us, St. Jude was like a light in the dark," she says.

The St. Jude team approach

Even though Sam's chemotherapy treatment was almost half as intense as Ben's had been, the child did not recover as quickly as he should have. Sanders immediately consulted with Amar Gajjar, MD, St. Jude Oncology co-chair. They determined that Sam's body must have a problem repairing the DNA damage caused by chemotherapy.

Russell Ware, MD, PhD, St. Jude Hematology chair, suggested that they test Sam to see if he had Fanconi anemia, a genetic disease that causes children to have an increased risk of cancer. The team collaborated with a physician in New York who runs the International Fanconi Registry. Sure enough, Sam had an extremely rare subtype of Fanconi anemia that involves a mutation of the *BRCA2* gene. Sanders suspects that Ben also had this genetic mutation, which heightened his susceptibility to the high-dose chemotherapy and hastened his death.

In trying to pinpoint the best possible treatment for Sam, Gajjar and Sanders also consulted with a researcher in the St. Jude Genetics and Tumor Cell Biology department, who was studying the *BRCA2* gene. Peter McKinnon, PhD, offered insights based on research he had conducted in the laboratory.

"Dr. McKinnon was able to give us a bigger, better perspective on how severe this disorder is," Sanders explains. "There are multiple checks and balances on the DNA damage-repair process, and *BRCA2* is one of the key elements. When *BRCA2* is damaged or missing, children don't have an ability to repair DNA, so radiation would cause the same kind of severe damage that the chemotherapy could cause."



Robert Sanders, MD, consulted with a researcher in Genetics and Tumor Cell Biology as he sought treatment options for Sam. "Not every hospital has a research tower full of people who spend their whole day trying to figure this stuff out," observes Sam's mom, Lisa.

Lisa and Brian were impressed by the level of cooperation involved in Sam's treatment.

"Dr. Sanders went to great lengths to talk with other doctors and figure out what was going on," Lisa says. "We know from experience that that doesn't happen in some other places. Also, not every hospital has a research tower full of people who spend their whole day trying to figure this stuff out. After Dr. Sanders met with Dr. McKinnon, they realized that they couldn't do radiation with Sam. If we hadn't figured that out, he could have been a vegetable, with total necrosis of his brain. I wouldn't have him here now."

Lessons learned

Sam's recent scans indicated no evidence of disease with no tumor growth. However, because the rare form of Fanconi anemia makes Sam supersensitive to chemotherapy and radiation, he cannot undergo additional treatment.

"There are not enough kids like Sam to really even have any quantifiable information about what kind of future they have," Lisa says. "My hope is that other children can benefit because of Sam and the knowledge that they're getting from him."

Sanders says clinicians are already learning valuable lessons from Sam's experiences. "Now that we know about the association with Fanconi, we can test for it," he says. "After Sam came, we had a patient with Wilms (a kidney tumor) that had some unusual features. They tested for Fanconi, and that patient has it, too." Sanders says Sam's case also underscores the need for genetic counseling for many St. Jude families. Meanwhile, McKinnon

and his team are continuing their investigations into the *BRCA2* gene.

Lisa and Brian are confident that their son is receiving the best possible care at St. Jude.

"I don't think another doctor and another hospital could have been as diligent or as cautious and caring and conscientious as Dr. Sanders and St. Jude have been," Lisa says. "Everybody in this place eats, sleeps and breathes these kids and the hope of getting them through one more day, through one more week, through forever.

"Because of the Fanconi, our picture is much different than when we first got here, but I still have hope for Sam. And that's because we're here. I know that if any place is going to give him the best shot at any sort of life, however long it might be, it's St. Jude." \bullet

Perspective

Tough Guys Love Kids, Too

"Through the years, St. Jude Children's Research Hospital was always, always on my mind. I heard about it, and it stuck like gum on my shoe."

By Tony Sirico



Tony Sirico and 8-year-old patient Gina Mulieri get acquainted during a St. Jude fundraiser in New York.

I'm an old tough guy. You've got problems? If I can help you, that's good. But a kid who has problems? I don't know why it is, but kids just get to me. And if they're sick, I'll do anything I can do to help them.

I was born during the war, and as a kid in the early '50s, I used to watch Danny Thomas on *Make Room for Daddy*. Later on, I heard that he had created a hospital for sick children with cancer and that he had named it after St. Jude—the patron saint of the hopeless. That was very important to me. Through the years, St. Jude Children's Research Hospital was always, always on my mind. I heard about it, and it stuck like gum on my shoe.

Early on in my acting career, I wasn't able to help the kids at St. Jude as much as I would have liked. I've struggled all my life, but I've gotten lucky these last several years, and I've devoted myself to giving it back. In my kitchen, I have pictures of kids who are being taken care of at St. Jude pictures that the hospital has sent me during the past six or seven years. When I walk into my kitchen in the morning, I say, "Hi, kids! Good morning!" Those pictures help me remember what those children are going through.

You see these beautiful little boys and girls with cancer. Every time I get a picture of one of them, I want to hug them and do everything I can to help. St. Jude is my pet charity, because of what they do for kids without asking for a dime from them. They run that hospital like a family. The doctors there are the best. They've even closed the gap on leukemia. All of that makes me feel good.

In the past few years, I've been trying to help the hospital as much as I can. All *The Sopranos* cast came to our first event back in 2005. Everybody dug, and they dug deep. I expected to raise maybe \$100,000 or \$200,000. But we raised nearly half a million dollars!

And then our charity event last summer was a real classy event. We raised more than \$600,000 for the hospital, and had a wonderful time going about it. But I haven't done any of these events by myself. My right hand and my best friend, Michael Sullivan, and his wife, Donna, have been a great influence and a big help in helping raise money for St. Jude. My other friend involved in St. Jude activities is Joe Scarpinito. His big heart and large pockets come through whenever I mention the kids, and God loves him for it. Just call us the three amigos. And our mission? The kids at St. Jude.

There are a lot of other people out here who love St. Jude. And there's more every day. The more people hear about the hospital and the kids, the more they want to give their hearts to it.

So tell all your friends that Tony Sirico, AKA Paulie Walnuts, says to take the boxing gloves off and dig deep into your pockets, because the kids need it. Just give them a hand; they really need your help. Thanks, and God bless.

Tony Sirico is known to millions as Paulie "Walnuts" Gualtieri on the Emmy award-winning HBO series The Sopranos. In addition to performing voice-overs for several children's programs, Sirico has appeared in more than 45 films. ●



Your legacy can be his future.

You can play a vital role in helping secure a healthy future for children battling cancer with a gift to St. Jude Children's Research Hospital[®] through your will. Join others who share the desire to leave a legacy of hope to catastrophically ill children by considering a bequest gift to St. Jude. To learn more about these special gifts and the Danny Thomas – St. Jude Society which recognizes these contributions, please call us at 800-395-1087, visit www.stjudelegacy.org or complete the enclosed postage paid envelope today.

Ensure that our research continues until the day we have conquered childhood cancer. The promise of your charitable legacy helps make it possible.

Finding cures. Saving children.





Miley Cyrus, who plays the TV character Hannah Montana, visited children at St. Jude while in Memphis for her "Best of Both Worlds" concert tour at FedExForum. Actor and musician Billy Ray Cyrus, Miley's father, has been a longtime supporter of St. Jude. Patients pictured with Cyrus are (from left, rear) Zoe Perkins, Bryce Reichert, Abigail Perez, Madelyn Beamon, Sebastien Louis-Fils and Madelynn Ellis.



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